IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **COOPER ET AL.**

Serial No. **10/609,019**

Filed: **June 26, 2003**

For: **GENE REGULATION IN TRANSGENIC ANIMALS USING A TRANSPOSON-BASED VECTOR**

Art Unit: **1632**

Examiner: **Anoop Singh**

Considered 90 11/2/06

considered 10/31/06

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

I, Richard K. Cooper, do hereby declare the following:

1. I am employed as a Professor in the Veterinary Science Department at the Louisiana State University AgCenter. In addition, I am the chief scientist for the company TransGenRx, which is actively involved in developing technologies for the generation of transgenic animals. In conjunction with my research responsibilities for the University and TranGenRx, I have been actively engaged in research relating to the development of transposase-based vectors for the development of transgenic animals, including birds.

2. I have reviewed the Office Action mailed June 26, 2006, in the above-referenced patent application and, in particular, the Examiner's rejection of claims under 35 U.S.C. § 103, at pages 3-10 of the Office Action.

3. The vectors described and claimed in the above-referenced patent application have provided surprising results in that the levels of incorporation of the transposon sequences and the gene of interest are much higher than any other transposon-based vectors of which I am aware. Based on comparisons to other vectors of which I am aware, the improved integration

frequency appears to result from the modifications made to the vector including positioning a Kozak sequence as part of the first codon for the prokaryotic transposase gene, the modifications to the beginning of the transposase gene, and the use of a polyA sequence operably linked to the prokaryotic transposase gene.

4. In addition to the experiments described in the patent application, the vectors described in the patent application have been used to incorporate a gene encoding a monoclonal antibody into both liver and the ovary genomic DNA of farm bred quail by intra-arterial administration. In this experiment, 7 week old quail were intra-cardiac injected with 20 μg DNA of a transposon-based vector of the invention (pTnMod) having a monoclonal antibody (MAb) as the gene of interest. Two days post-injection, DNA was isolated from tissues for analysis by PCR. PCR assays were performed on liver and ovary DNA with primers designed to amplify the monoclonal antibody gene sequences. A portion of the PCR sample was visualized on a 1.5% agarose gel stained with ethidium bromide. The results are shown as Exhibit A, showing incorporation of the monoclonal antibody gene in the DNA of the livers of G0 animals, and Exhibit B, showing incorporation of the monoclonal antibody gene in the DNA of the ovary and liver of G0 animals. Exhibits A and B are attached to this declaration.

5. Samples on the gel in Exhibit A are as follows.

Lanes	Sample
1	100 base pair ladder
2-6	liver from individual quail (farm-1) injected with the MAb/pTnMod vector
7	liver from a quail (farm-1) not injected with the MAb/pTnMod vector
8-12	liver from individual quail (farm-2) injected with the MAb/pTnMod vector
13	liver from a quail (farm-2) not injected with the MAb/pTnMod vector
16-17	DNA negative PCR controls
18	blank lane
19	positive vector control
20	100 base pair ladder

6. Ovaries were isolated from the birds used in the experiment shown as Exhibit A and DNA isolated from the tissue for PCR amplification of the MAb gene sequence. A portion of the PCR sample was visualized on a 1.5% agarose gel stained with ethidium bromide. The

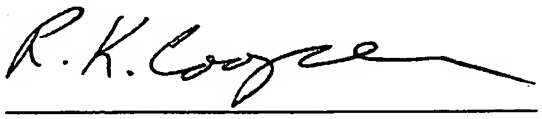
results are shown as Exhibit B. As noted in the gel of Exhibit B, 100% of the birds are positive for incorporation of the MAb gene.

7. Samples on the gel in Exhibit B are as follows.

Lanes	Sample	Lane	Sample
1	DNA ladder -1	11	quail 2890 ovary
2	quail 2201 liver	12	quail 2892 ovary
3	quail 2201 ovary	13	quail 2893 ovary
4	quail 2204 ovary	14	quail 2211 ovary negative control
5	quail 2206 ovary	15	quail 2895 ovary negative control
6	quail 2207 ovary	16	DNA extraction kit control
7	quail 2209 ovary	17	DNA extraction kit control
8	quail 2596 liver	18	No DNA control
9	quail 2596 ovary	19	positive vector control
10	quail 2598 ovary	20	DNA ladder 2

8. The results demonstrate the high level of incorporation of the MAb DNA into the genomic DNA from ovarian tissue and liver tissue isolated from the treated quail. When the same samples were analyzed for transposase nucleic acid sequences very little transposase DNA was detected, indicating that most of the vector had been destroyed.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



09/25/2006
Date

Richard K Cooper, Ph.D.

Exhibit A

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

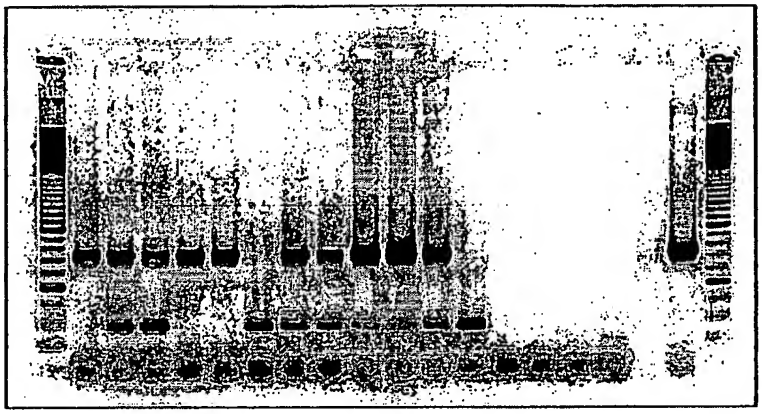


Exhibit B

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20